Haemophilus b conjugate vaccine

A new conjugate vaccine to protect against meningitis and other systemic infections caused by *Haemophilus influenzae* type b (Hib), which can be used in children as young as 18 months of age, was licensed Feb. 2, 1988, for use in Canada. It is composed of the purified capsular polysaccharide (PRP) of Hib covalently bound to diphtheria toxoid (D). The advantages of PRP-D over the previously licensed polysaccharide vaccine (PRP) are presented here, as are recommendations for the use of PRP-D.

Haemophilus b conjugate vaccines represent the second generation of vaccines protecting against diseases caused by Hib and are designed to take advantage of the greater immune responses of infants and young children to polysaccharide–protein conjugate antigens than to the antigens of the original pure polysaccharide vaccines. Unlike the old vaccines, which stimulate only B cells, the new ones activate macrophages and helper T cells as well, for a greatly enhanced antibody response.

Because of the increased immunogenicity of PRP-D the recommended age of the recipients can be lowered from 24 to 18 months.[1-3] This change will protect an additional 10% of children at risk against invasive Hib disease. Between 35% and 40% of the cases of invasive disease occur in the age groups that will now be eligible for vaccination.

Each dose of PRP-D contains 25 μg of polysaccharide covalently bound to 18 μg of diphtheria toxoid in 0.5 ml of phosphate-buffered saline and thimerosal (1:10 000) as a preservative. The amount of diphtheria toxoid is insufficient for primary or booster immunization against diphtheria, so the conjugate vaccine should not be used for that purpose.

Advantages

PRP-D induces greater amounts of antibody in infants and young children than does PRP. Either vaccine produces significantly greater antibody responses in children with pre-existing anti-PRP antibody than in those without the antibody. The use of diphtheria toxoid as the carrier protein results in enhanced anti-PRP antibody responses when children previously immunized with the toxoid are first given PRP-D. More than 90% of children vaccinated with PRP-D between the ages of 15 and 24 months produced protective antibody levels (0.15 μg/ml or greater), as compared with less than 50% of children given PRP at this age.[3] Twice as many PRP-D recipients (60% v. 30%) had antibody levels considered indicative of long-term protection (1.0 μg/ml or greater).[3]

The use of PRP-D in children 18 months of age is recommended on the basis of the vaccine's superior immunogenicity, as measured by antibody production, rather than its demonstrated protective efficacy. However, the relation between the magnitude of the antibody response and the protective efficacy has been established in trials with PRP vaccine.[4]

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Additional advantages of PRP-D include longer persistence of antibody and the establishment of immunologic memory, which allows anamnestic or accelerated antibody responses to occur when the vaccine recipient subsequently encounters capsular polysaccharide, either naturally or as a booster. Antibody produced in response to conjugate vaccine is biologically equivalent to that produced in response to polysaccharide vaccine.

Recommended use

- A single dose of PRP-D is recommended for routine vaccination of all children at 18 months of age.
- Children aged 19 to 24 months who have not received any Hib vaccine should be given PRP-D.
- PRP-D vaccination should be considered in children aged 25 to 60 months, especially younger children, those attending day-care centres and those at increased risk of invasive Hib disease because of sickle-cell disease, anatomic or functional asplenia, partial immunoglobulin deficiency or immunosuppression (although responsiveness in immunocompromised children has not been confirmed).
- Children more than 5 years of age who have chronic conditions associated with an increased risk of invasive Hib disease may be given PRP-D.
- Children who have had invasive Hib disease before 18 months of age should still be given PRP-D, because the disease may not have rendered them immune.
- Children who have received PRP do *not* require a booster dose of PRP-D unless PRP had been given before 24 months of age. A single booster dose of PRP-D should be given if the children are still at increased risk of Hib disease. There should be an interval of at least 2 months between the doses.
- PRP-D can be administered simultaneously with diphtheria–pertussis–tetanus (DPT) or DPT–polio vaccine, at separate sites with separate syringes. Data are lacking on the concomitant use of PRP-D and measles–mumps–rubella (MMR) vaccine.[5] However, if the patient is unlikely to return for further vaccination, simultaneous administration of all the required vaccines is recommended.
- Immunization does not prevent acquisition and carriage of Hib; therefore, vaccinated children who have been exposed to Hib infection should receive rifampin, in the recommended dosages, to prevent secondary cases in families and day-care centres.

PRP-D is *not* recommended for use in infants less than 18 months of age, because its effectiveness has not been confirmed. The need for booster doses of conjugate vaccine has not been established.

Adverse reactions

Up to 7% of infants vaccinated at 16 to 24 months of age have suffered local erythema, induration and tenderness;[3] slight temperature increases have occurred in 24% of the infants, but the temperature has risen above 39.0°C in only 0.7%. Irritability has been noted in 16%.[3] The rates of local and systemic reactions in children given PRP-D have not been significantly greater than the rates in those given a placebo.[3] In a trial of more than 30 000 infants who were given three doses of PRP-D between 3 and 6 months of age no severe adverse reactions were reported.[6]

Contraindications

PRP-D should not be given to children with acute febrile illness or to those who are allergic to any component of the vaccine.

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